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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/725,607	12/02/2003	Roger Akers	SYNT-P003US	4955

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EXAMINER	
BOWERS, NATHAN ANDREW	
ART UNIT	PAPER NUMBER
1797	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/725,607	AKERS ET AL.	
	Examiner	Art Unit	
	Nathan A. Bowers	1797	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18, 23 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *18 and 23* is/are allowed.

6)☒ Claim(s) *1 and 3-12* is/are rejected.

7)☒ Claim(s) *2,13-17 and 24* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 24 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Section (e) in claim 24 should instead be grouped under the heading section (iii). Applicant discloses a plurality of membrane carrier assemblies wherein each membrane carrier assembly comprises a (i) support cylinder and (ii) a molecular weight cut-off membrane. After review of Applicant's specification, each membrane carrier assembly additionally comprises (iii) a chamber between the exterior surface of the cylinder and an interior surface of the membrane. Thus, the claim should reflect this relationship, and clearly indicate that each membrane carrier assembly includes and is individually associated with a separate chamber.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1) Claims 1, 7, 8 and 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schwarz (US 5155035) in view of Bauer (US 6107055).

With respect to claims 1, 10 and 11, Schwarz discloses a culture chamber comprising a tubular housing (Figure 3:20), a growth compartment (Figure 3:30) within the housing, a fluid inlet (Figure 2:67) and a fluid outlet (Figure 2:86). A membrane carrier assembly transversing the growth compartment is additionally provided. The carrier assembly includes a support cylinder divided into a first end (Figure 2:23) and a second end (Figure 2:25). The first end is in communication with the fluid inlet, and the second end is in communication with the fluid outlet.

A filter (Figure 2:35) is secured to the exterior surface of the support cylinder in order to form a chamber (Figure 2:85) between the exterior surface of the cylinder and the interior surface of the membrane. This is described in column 7, line 36 to column 8, line 62. However, it is not clear if the filter disclosed by Schwarz is a molecular weight cut-off membrane.

Bauer discloses a culture chamber comprising a plurality of molecular weight cut-off membranes (Figure 1:10 and Figure 1:7) that are used to separate valuable cell products from the rest of the fermentation solution. This is described in column 1, lines 46-67, column 4, lines 18-26 and column 5, lines 17-46. Bauer indicates that only compounds of 100,000 daltons or less are allowed to perfuse through the membranes.

Schwarz and Bauer are analogous art because they are from the same field of endeavor regarding cell culture chambers.

At the time of the invention, it would have been obvious to ensure that the filter disclosed by Schwarz is a molecular cut-off membrane similar in design to those described by Bauer. Bauer teaches that molecular cut-off membranes are useful in collecting valuable cell products, removing wastes, and retaining cells within the culture chamber. As evidenced by Bauer, the use of separation membranes in cell culture apparatuses is well known in the art, and it would have been apparent to implement them in the construction of Schwarz's bioreactor.

With respect to claims 7 and 8, Schwarz and Bauer disclose the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above. In addition, Schwarz teaches that the fluid inlet and outlets are connected to the housing through fluid conducting swivels. In column

7, line 49 to column 8, line 28, Schwarz teaches that the support cylinder is mounted to the housing in a rotatable fashion.

With respect to claim 12, Schwarz and Bauer disclose the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above. It is clear from the Figures that the bioreactor of Schwarz is generally cylindrical and symmetrical in shape..

2) Claims 3-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schwarz (US 5155035) in view of Bauer (US 6107055) and further in view of Schwarz (US 5026650).

With respect to claim 3, Schwarz '035 and Bauer disclose the apparatus as previously described in the 35 U.S.C. 103 rejections above, however do not expressly indicate that the housing and support cylinder each have respective first and second end cap fittings.

Schwarz '650 discloses the apparatus as previously described above. Schwarz teaches that the apparatus includes first and second end fittings (Figure 1:20) sealingly fit within the bore of the sleeve and each include an interior projection. The end fittings include nozzles connected to through bores capable of adding and removing gases, as well as counterbores capable of holding the support cylinder. Schwarz additionally indicates that the membrane carrier assembly includes a support cylinder comprising first and second end plugs (Figure 2:35a). The end plugs have a through hole in communication with the through bore of the housing end fittings, and are positioned within the counterbores of the end fittings. See Figure 2.

Schwarz '035, Bauer and Schwarz '650 are analogous art because they are from the same field of endeavor regarding cell culture apparatuses.

At the time of the invention, it would have been obvious to provide the housing and support cylinder disclosed by Schwarz '035 each with end caps members and associated connecting means. Schwarz '650 indicates that end caps are beneficial because they can be fitted with through bores useful in the transport of fluids to and from the interior of the vessel. Schwarz '650 also indicates that the end caps of the cylinder support can be fitted within bores of the housing end caps to ensure that the cylinder support is securely attached to the remainder of the housing structure. The implementation of end caps and corresponding bores would not require significant structural design set forth by Schwarz '035.

With respect to claims 4-6, Schwarz '035, Bauer and Schwarz '650 disclose the apparatus set forth in claim 3 as set forth in the 35 U.S.C. 103 rejection above. In addition, Schwarz '035 indicates in column 14, lines 15-25 that a venting port is used to purge gases from the culture chamber. These ports are also fully capable of being used to transfer fluids to and from the housing.

3) Claim 9 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schwarz (US 5155035) in view of Bauer (US 6107055) as applied to claim 1, and further in view of Falkenberg (US 5576211).

Schwarz and Bauer disclose the apparatus set forth in claim 1 as set forth in the 35 U.S.C. 103 rejection above, however do not expressly disclose that the molecular weight cut-off membrane is dialysis tubing.

Falkenberg discloses a culture vessel comprising a tubular housing that contains a dialysis tubing membrane (Figure 5:22). Column 7, lines 22-56 indicate that the dialysis tubing retains the cell culture while allowing the diffusion of nutrients and gases.

Schwarz, Bauer and Falkenberg are analogous art because they are from the same field of endeavor regarding cell culture systems.

At the time of the invention, it would have been obvious to ensure that the membrane used in the system of Schwarz was a dialysis tubing membrane. Falkenberg teaches that dialysis tubing is beneficial because it allows metabolic cell products to be removed from the culture system while retaining the remainder of the culture solution. One of ordinary skill would understand that the molecular weight cut-off membrane set forth by Bauer, the filter disclosed by Schwarz, and the dialysis tubing described by Falkenberg are all functionally equivalent separation devices, and that it would have been apparent to interchange Schwarz's filter with either of these membranes. Furthermore, the use of dialysis tubing is considered to be well known in the art.

Terminal Disclaimer

The terminal disclaimer filed on 03 December 2007 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of U.S. Patent Number 7,144,727 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Allowable Subject Matter

Claims 2 and 13-17 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

With respect to claim 2, the prior art does not in the claimed environment disclose a plurality of membrane carrier assemblies each transversing the growth compartment and each including a support cylinder, a molecular weight cut-off membrane, and a chamber containing circulating culture medium. The Schwarz '035 and Schwarz '650 references represent the closest prior art, but each only disclose a single membrane carrier assembly. The addition of multiple membrane carrier assemblies such that each assembly transverses the growth compartment would require significant structural alterations to the Schwarz apparatuses, and accordingly represents an inventive improvement. The prior art does not disclose a bioreactor comprising a plurality of membrane carrier assemblies of the nature claimed by Applicant.

With respect to claims 13-17, the prior art does not in the claimed environment disclose a support cylinder comprising a blind hole in communication with a plurality of radial cross holes extending to the exterior surface of the cylinder. As persuasively argued by Applicant, the Schwarz '650 reference only discloses the use of a single radial cross hole in communication with a blind hole. The current invention uses multiple radial cross holes to evenly distribute the circulating fluid through the liquid circulation system, whereas the single cross hole of Schwarz '650 creates pressure on one side of the membrane and therefore does not allow for the optimum diffusion of biochemicals through the membrane.

Claims 18 and 23 allowed.

With respect to independent claim 18, prior art does not in the claimed environment disclose a support cylinder comprising a blind hole in communication with a plurality of radial cross holes extending to the exterior surface of the cylinder to create a plurality of surface pockets. As persuasively argued by Applicant, the Schwarz '650 reference only discloses the use of a single radial cross hole in communication with a blind hole. The current invention uses multiple radial cross holes to evenly distribute the circulating fluid through the liquid circulation system, whereas the single cross hole of Schwarz '650 creates pressure on one side of the membrane and therefore does not allow for the optimum diffusion of biochemicals through the membrane.

Claim 24 would be allowable if rewritten or amended to overcome the rejection under 35 U.S.C. 112, 2nd paragraph, set forth in this Office action.

With respect to claim 24, the prior art does not in the claimed environment disclose a plurality of membrane carrier assemblies each transversing the growth compartment and each including a support cylinder, a molecular weight cut-off membrane, and a chamber containing circulating culture medium. The Schwarz '035 and Schwarz '650 references represent the closest prior art, but each only disclose a single membrane carrier assembly. The addition of multiple membrane carrier assemblies such that each assembly transverses the growth compartment would require significant structural alterations to the Schwarz apparatuses, and accordingly

represents an inventive improvement. The prior art does not disclose a bioreactor comprising a plurality of membrane carrier assemblies of the nature claimed by Applicant.

Response to Arguments

Applicant's arguments filed 03 December 2007 with respect to the 35 U.S.C. 102 rejections involving Schwarz '650 have been fully considered and are persuasive. These rejections have been withdrawn.

Applicant's arguments filed 03 December 2007 with respect to the 35 U.S.C. 103 rejections involving Schwarz '650, Bauer and Kersten have been fully considered and are persuasive. These rejections have been withdrawn.

Applicant's arguments filed 03 December 2007 with respect to the 35 U.S.C. 103 rejection involving Schwartz '035 and Bauer '055 have been fully considered but they are not persuasive.

Applicant's principle arguments are

(a) Schwarz does not disclose a support cylinder that transverses the growth compartment.

In response to Applicant's arguments, please consider the following comments.

The support cylinder of Schwarz does transverse the growth compartment because the carrier assembly includes a support cylinder divided into a first end (Figure 2:23) and a second end (Figure 2:25). The first end is in communication with the fluid inlet, and the second end is

in communication with the fluid outlet. Although it is agreed that the support cylinder of Schwarz is discontinuous, a single, unbroken support cylinder is not required by the claims. To "transverse" simply means "to cross from side to side." Although discontinuous through the middle, the support cylinder of Schwarz is clearly positioned at each side of the growth compartment.

Applicant's principle arguments are

(b) Schwarz does not disclose a molecular weight cut-off membrane.

In response to Applicant's arguments, please consider the following comments.

It is agreed that Schwarz discloses a filter, but not necessarily a molecular weight cut-off membrane. However, it would have been obvious to ensure that the filter is specifically a molecular weight cut-off membrane upon review of Bauer. The Bauer reference clearly discloses a culture chamber comprising a plurality of molecular weight cut-off membranes (Figure 1:10 and Figure 1:7) that are used to separate valuable cell products from the rest of the fermentation solution. Bauer teaches that molecular cut-off membranes are useful in collecting valuable cell products, removing wastes, and retaining cells within the culture chamber. As evidenced by Bauer, the use of separation membranes in cell culture apparatuses is well known in the art, and it would have been apparent to implement them in the construction of Schwarz's bioreactor.

Applicant's principle arguments are

(c) Schwarz and Bauer do not disclose a chamber bordered on one side by the exterior surface of the cylinder and on an opposed side by an interior surface of the membrane.

In response to Applicant's arguments, please consider the following comments.

Schwarz and Bauer each disclose chambers bordered on one side by the exterior surface of the cylinder and on an opposed side by an interior surface of the membrane. This is clear from Figure 2 of Schwarz

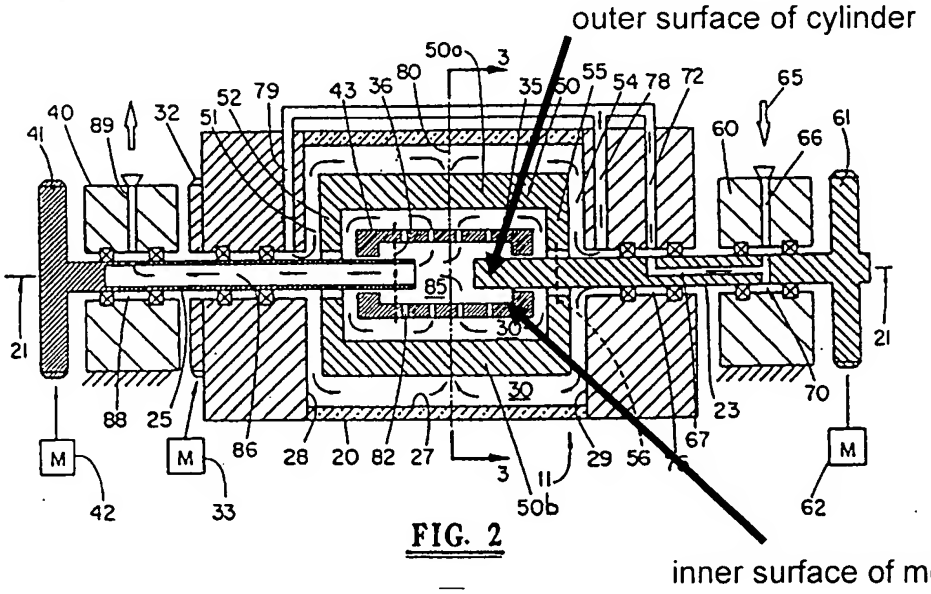

FIG. 2

Even though the cylinder of Schwarz is discontinuous, it still includes a region that comprises an outer surface that borders the chamber.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nathan A. Bowers whose telephone number is (571) 272-8613. The examiner can normally be reached on Monday-Friday 8 AM to 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gladys Corcoran can be reached on (571) 272-1214. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

NAB

GLADYS JP CORCORAN
SUPERVISORY PATENT EXAMINER